

6/8/01

SEQ ID NO:39, or a variant thereof, wherein the variant comprises an amino acid substitution at amino acid positions 5, 6, or both 5 and 6.

Remarks

The Amendments

The new Sequence Listing does not add new matter. It merely adds sequences that had been properly incorporated into the specification by reference. The Sequence Listing information recorded in the computer readable form is identical to the written sequence listing.

These sequences were incorporated into the specification by reference to, *inter alia*, U.S. Patent Application 09/146,400 filed 9/3/1998. SEQ ID NO:4 of U.S. Patent Application 09/146,400, which comprises exon 3 of canine IgE has been added into the text of the present application as SEQ ID NOs:33-39. Reference to newly added SEQ ID NOs:33-39 has been added to page 24 of the specification. The amendment adds no new matter.

Claims 1, 2, 7, 9-11, 16, 17, 22, 23, 28, 29, 30, 35, 36, 37, and 42 have been canceled. As recognized by the Office Action claims 9-11, 17, 23, 28, 30, 35, and 37 were intended to be canceled in the Response of October 19, 2001 and were not canceled in response to the pending rejections in the instant Office Action. Claims 1, 2, 7, 16, 22, 29, 36, and 42 are canceled herein; however, Applicants reserve the right to prosecute these claims, and all canceled claims, without prejudice in a continuing application.

Claims 6, 15, 21, 27, and 34 have been amended to recite that a specific binding protein that specifically binds to a peptide consisting essentially of a certain amino acid sequence. This amendment is made to clarify that the recited sequences do not comprise

sequences that are heterologous to canine IgE sequences. Claim 43 has been amended to delete the term “defined”. This amendment does not narrow the claim.

Claim 15 has been amended to correct the amino acid positions at which amino acid variations can occur. The specification teaches that these positions can be altered at page 10, lines 16-23. This is not a narrowing amendment and merely corrects the position numbers.

New claims 116 and 117 have been added. They recite a specific binding protein that binds SEQ ID NO:39 or specific variants thereof. SEQ ID NO:39 is Exon 3a, the 71 C-terminal amino acids of canine IgE. Support for the amendment can be found in the specification at, *inter alia*, page 24, lines 13-20 and page 10, lines 16-23.

These amendments do not constitute new matter. A marked-up copy of the amendments appears in attached Appendix A.

Objection to Drawings

Formal drawings are enclosed herein. Applicant respectfully requests withdrawal of the objection.

Objection to Claims 9, 11, 28, and 35

The Office Action has objected to claims 9, 11, 28, and 35. These claims have been canceled. Therefore, Applicants respectfully request withdrawal of the objection.

Rejection of Claims 17, 23, 30, 37, and 41 Under 35 U.S.C. §112, second paragraph

Claims 17, 23, 30, 37, and 41 stand rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite. Claims 17, 23, 30, and 37 have been canceled. As such, the rejection is moot as applied to these claims. Applicants traverse the rejection as it applies to claim 41.

The Office Action asserts that the recitation of “8H.8” renders the claim ambiguous. Applicants believe that the term is not ambiguous when read in light of the specification. However, in order to advance prosecution, the Applicants have deposited a hybridoma producing the 8H.8 monoclonal antibody with the ATCC and have added the ATCC designation number PTA-4597 to claim 41 and to the specification. A copy of the “Receipt in the case of an original deposit issued pursuant to rule 7.3 and viability statement issued pursuant to Rule 10.2” is attached to this response.

A declaration signed by Applicants is attached as Appendix B. The declaration states that a hybridoma that produces a monoclonal antibody described as “8H.8” in this patent application has been deposited with the American Type Culture Collection (ATCC) 10801 University Blvd., Manassas, Virginia 20110, USA, under the terms of the Budapest Treaty on August 13, 2002. The hybridoma has been received by the ATCC and reference number PTA-4597 has been assigned to the hybridoma. The hybridoma deposited with the ATCC on August 13, 2002 has been in the custody and control of IDEXX Laboratories since at least April 9, 1998 and the hybridoma deposited with the ATCC on August 13, 2002 is the same material that was in the possession of IDEXX Laboratories since at least April 9, 1998. This 8H.8 producing hybridoma is the same as that described in U.S. Patent Application Ser. No. 09/281,760. The hybridoma that produces 8H.8 monoclonal antibody will be irrevocably and without restriction or condition released to the public upon issuance of a patent. The deposit will be maintained by the ATCC for a period of 30 years after the date of the deposit, 5 years after the last request for a sample, or for the enforceable life of the patent, whichever is longer.

Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 41-43 Under 35 U.S.C. §112, first paragraph

Claims 41-43 stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking written description. Claim 42 has been cancelled. Applicants respectfully traverse the rejection as it applies to claims 41 and 43.

The Office Action asserts that the production of an 8H.8 monoclonal antibody using the C-terminal 71 amino acids of exon 3 of canine IgE is an unpredictable event and therefore asserts that a hybridoma which is capable of producing an 8H.8 monoclonal antibody must be deposited under the terms of the Budapest Treaty. Applicants respectfully disagree and assert that one of skill in the art could produce an 8H.8 antibody in light of the teachings of the specification. However, in order to advance prosecution, Applicants have deposited an 8H.8 monoclonal antibody producing hybridoma under the terms of the Budapest Treaty as described above and in attached Appendix B.

The Office Action further asserts that the C-terminal 71 amino acids of exon 3 of canine IgE is an essential material. The sequence was incorporated into the specification by reference to, *inter alia*, U.S. Patent Application 09/146,400 filed 9/3/1998. SEQ ID NO:4 of U.S. Patent Application 09/146,400, which comprises exon 3 of canine IgE has been added into the text of the present application as SEQ ID NOs:33-39. Reference to newly added SEQ ID NOs:33-39 has been added to page 24 of the specification.

A declaration signed by a practitioner representing the Applicants is attached as Appendix C. The declaration states that the amendatory material that has been incorporated by reference consists of the same material incorporated by reference in the referencing application.

Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-2, 6-11, 15-17, 21, 23, 27-30, 34-37, and 41-43 Under 35 U.S.C. §112, first paragraph

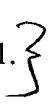
Claims 1-2, 6-11, 15-17, 21, 23, 27-30, 34-37, and 41-43 stand rejected under 35 U.S.C. §112, first paragraph as allegedly not enabled. Claims 1, 2, 7, 9, 10, 11, 16, 17, 23, 28, 29, 30, 35, 36, 37, and 42 have been canceled. As such, the rejection is moot as applied to these claims. Applicants respectfully traverse the rejection as it applies to claims 6, 8, 15, 21, 27, 34, 41 and 43.

The amended claims recite a specific binding protein selected from the group consisting of a monoclonal antibody, a polyclonal antibody, an antigen-binding fragment of a monoclonal antibody, an antigen-binding fragment of a polyclonal antibody, a hybrid antibody, and a single chain antibody which specifically binds an isolated and purified peptide comprising an amino acid sequence which consists essentially of Thr-Leu-Leu-Glu-Tyr-Arg-Met (SEQ ID NO:4), or a variant thereof, wherein the variant comprises an amino acid substitution at amino acid positions 3, 4, or both 3 and 4. The claims also recite a specific binding protein selected from the group consisting of a monoclonal antibody, a polyclonal antibody, an antigen-binding fragment of a monoclonal antibody, an antigen-binding fragment of a polyclonal antibody, a hybrid antibody, and a single chain antibody, which specifically binds an isolated and purified peptide comprising an amino acid sequence which consists essentially of Gly-Met-Asn-Leu-Thr-Trp-Tyr-Arg-Glu-Ser-Lys (SEQ ID NO:5), or a variant thereof, wherein the variant comprises an amino acid substitution at amino acid position number 5, 6, or both 5 and 6. The claims also recite a monoclonal antibody produced by hybridoma 8H.8 having ATCC accession number PTA-4597.

The amended claims are enabled by the specification. Under 35 U. S. C. § 112, all that is required is that the specification describe the invention in such terms as to enable a person skilled in the art to make and use the invention. Thus, the specification must teach one skilled in the art how to make and use a 8H.8 monoclonal antibody and the claimed specific binding proteins. The test of enablement is whether one reasonably skilled in the art (1) could make and use the invention (2) from the disclosures in the patent coupled with information known in the art (3) without undue experimentation. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988); *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); M.P.E.P. § 2164.01. “The determination of what constitutes undue experimentation is a given case requires the application of a standard of reasonableness, having due regard of the nature of the invention and the state of the art.” *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) (citing *Ansul Co. v. Uniroyal, Inc.*, 169 U.S.P.Q. 759, 762-63 (2d Cir. 1971). “The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.” *Id.*

The specification teaches how to make and use an 8H.8 monoclonal antibody. Additionally, a hybridoma that produces an 8H.8 monoclonal antibody has been deposited under the terms of the Budapest treaty. As such one of skill in the art could make an 8H.8 antibody. The specification teaches that the monoclonal antibody can be used to, for example, target IgE. See, e.g., specification page 20, line 10 through page 23, line 20.

The Office Action additionally asserts that the specification does not enable a specific binding protein that specifically binds a peptide comprising SEQ ID NOs:1-5. Claims 6, 15, 21, 27, and 34 have been amended to recite specific binding proteins that specifically bind to a peptide consisting essentially of a defined amino acid sequence. The transitional phrase “consisting essentially of” means that the defined amino acid sequence is covered by the claim and any other materials that do not materially affect the basic and novel characteristics of the claim. *See* MPEP §2111.03; *In re Herz*, 190 USPQ 461,463 (CCPA 1976). The basic and novel characteristics of the defined amino acid sequences of the invention are that a monoclonal antibody, 8H.8, specifically binds to these sequences. The specification enables specific binding proteins that bind to a peptide consisting essentially of SEQ ID NO:4 or a variant thereof, wherein the variant comprises an amino acid substitution at amino acid positions 3, 4, or both 3 and 4 and SEQ ID NO:5, or a variant thereof, wherein the variant comprises an amino acid substitution at amino acid position number 5, 6, or both 5 and 6.

One of skill in the art, given the specification could make and specific binding proteins that specifically bind to SEQ ID NO:4 and SEQ ID NO:5, and specific variants thereof. Specific binding proteins as defined in the specification at page 17, lines 16-22 were well known in the art at the time the application was filed. It was also well known how to make a specific binding protein that could specifically bind to a defined amino acid sequence. For example, a monoclonal antibody, which is a specific binding protein, was generated as described at page 24, lines 13-20. The specification also teaches that specific binding proteins can be used for, *inter alia*, diminishing the production of IgE in a dog. See, e.g., page 32, lines 3-11. 

The Office Action asserts that the specification does not enable an antibody that can bind any variant caused by a non-conservative mutation. The claims recite amino acid sequences of Thr-Leu-Leu-Glu-Tyr-Arg-Met (SEQ ID NO:4), or a variant thereof, wherein the variant comprises an amino acid substitution at amino acid positions 3, 4, or both 3 and 4 and amino acid sequences of Gly-Met-Asn-Leu-Thr-Trp-Tyr-Arg-Glu-Ser-Lys (SEQ ID NO:5), or a variant thereof, wherein the variant comprises an amino acid substitution at amino acid position number 5, 6, or both 5 and 6.

The specification clearly teaches that positions 3 and 4 of SEQ ID NO:4 and positions 5 and 6 of SEQ ID NO:5 can be any amino acid. The amended claims recite that specific binding proteins of the invention specifically bind to purified peptides comprising SEQ ID NO:4, SEQ ID NO:5 or variants thereof. The variants are defined in the claims as amino acid substitutions at amino acid positions 3, 4, or both for SEQ ID NO:4 and at amino acid positions 5, 6, or both for SEQ ID NO:5. The specification clearly teaches that substitutions can be made within a core sequence of SEQ ID NO:4 or SEQ ID NO:5. Specifically, the specification teaches that a core peptide sequence comprises Leu-Xaa-Xaa-Tyr-Arg (SEQ ID NO:1). See page 10, lines 16-23. Both SEQ ID NOs:4 and 5 comprise the core sequence of SEQ ID NO:1 and can therefore comprise substitutions between the core Leu residue and the Tyr-Arg pair. The specification also provides assays that can be used to determine if a variant peptide specifically binds a specific binding protein of the invention. See Example 2.

Therefore, one of skill in the art could make the claimed variants of SEQ ID NO:4 and SEQ ID NO:5 and could test and use specific binding proteins that bind to the variant peptides. As such the claimed variants are enabled by the specification.

The Office Action alleges that due to ambiguity of the identity of the antibody of claim 41, one of skill in the art would not know which epitopes are recognized by the antibody in claim 43. Amended claim 41 recites a specific monoclonal antibody that is produced by a specific hybridoma. One of skill in the art, given the teachings of the specification, could identify epitopes bound by the antibody of claim 41.

The Office appears to be concerned about the number of epitopes that could conceivably specifically bind to an 8H.8 monoclonal antibody. However, the enablement inquiry is whether one of skill in the art could make and use a specific binding protein of the invention given the teachings of the specification and knowledge of those of skill in the art at the time the invention was made. One of skill in the art could easily determine whether an 8H.8 antibody bound a specific epitope using guidance provided in the specification and techniques well known in the art. As such, the claims are enabled by the specification. Applicant respectfully requests withdrawal of the rejection.

Rejection of Claims 1-2, 6-11, 15-17, 21, 23, 27-30, and 34-37 Under 35 U.S.C. §112, first paragraph

Claims 1-2, 6-11, 15-17, 21, 23, 27-30, and 34-37 stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking written description. Claims 1, 2, 7, 9, 10, 11, 16, 17, 22, 23, 28, 29, 30, 35, 36 and 37 have been canceled. As such, the rejection is moot as applied to these claims. Applicants respectfully traverse the rejection as it applies to claim 6, 8, 15, 21, 27, and 34.

The standard for written description whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, the Applicant

was in possession of the invention as now claimed. *See Vas-Cath, Inc. v. Mahurkar*, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991). An Applicant shows possession of the claimed invention with all of its limitations using such descriptive words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *See Lockwood v. American Airlines, Inc.*, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997).

The Office Action asserts that Applicants are not in possession of any antibody specific for any genus of peptides “comprising” SEQ ID NOs:4-5 or any other genus of undefined peptides comprising any other undefined sequence. The claims have been amended to recite peptides that consist essentially of SEQ ID NOs:4-5 and specific variants thereof. The meaning and support for “consisting essentially of” has been discussed above. One of skill in the art would recognize that Applicants were in possession of specific binding proteins that specifically bind peptides “consisting essentially of” SEQ ID NOs:4-5 and specifically defined variants thereof.

The specification clearly defines SEQ ID NO:4 and SEQ ID NO:5 and specific variants thereof. As such the claims are enabled and Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-2, 6-11, 15-16, 21-22, 27-29, and 34-36 Under 35 U.S.C. §103(a)

Claims 1-2, 6-11, 15-16, 21-22, 27-29, and 34-36 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent 5,514,776 (the ‘776 patent) in view of U.S. Patent 5,629,415 (the ‘415 patent). Claims 1, 2, 7, 9-11, 16, 22, 28, 29, 35, and 36 have been canceled. As such, the rejection is moot as applied to these claims. Applicants respectfully traverse the rejection as it applies to claims 6, 8, 15, 21, 27, and 34.

The Office Action asserts that the '776 patent teaches monoclonal antibodies that bind to canine B cell membrane-bound immunoglobulins, but do not induce histamine release from basophils and mast cells. The Office Action recognizes that the '766 patent does not teach antibodies that recognize SEQ ID NOS:4 or 5. The Office Action further asserts that the '415 patent teaches specific binding proteins that can bind to full-length canine IgE or peptide fragments of IgE. The Office Action further asserts that the '415 patent teaches that such antibodies may be important in inhibition of binding of IgE to its receptor on mast cells to provide a way to control allergic responses.

The '776 patent teaches antibodies that bind to an €.mb/ec peptide which is shown in SEQ ID NO:2. See Col. 7, lines 22-27; Col. 4, lines 20-51. The €.mb/ec peptide (SEQ ID NO:2) does not have homology to SEQ ID NOS:4 and 5 of the instant invention. As such, the '776 patent does not teach or suggest or specific binding proteins that specifically bind the peptides recited in claims 6, 8, 15, 21, 27, and 34 of the instant invention.

The '415 patent does not teach or suggest SEQ ID NO:4 of the instant invention. Furthermore, the '415 patent does not teach or suggest the use of distinct peptides as shown in SEQ ID NOS:4 and 5. Therefore, the '415 patent does not teach, suggest, or inherently disclose the specific, individual polypeptides shown in SEQ ID NOS:4 and 5 and does not identify the polypeptide fragments to be of any particular use. There is no teaching in the '415 patent, directly or inherently, that would direct one of skill in the art to the particular defined sequences of SEQ ID NOS:4 and 5 for any reason. The '415 patent does not teach or suggest that SEQ ID NOS:4 and 5 are sequences that would be useful as individual peptides apart from entire protein sequence. The '415 patent

provides no recognition or suggestion that the distinct polypeptides shown in SEQ ID NOs:4 and 5 or any other specific polypeptide fragments would be useful to generate specific binding proteins that specifically bind to native canine B cell-bound IgE and which do not bind to IgE when the IgE is bound to a receptor on a mast cell.

Additionally, the '415 patent does not teach or suggest SEQ ID NO:4 of the instant invention. Claims 21, 27, and 34 have been amended to recite that the claimed binding proteins specifically bind to an isolated and purified amino acid sequence which *consists essentially of* SEQ ID NO:5.

Therefore the '776 patent in view of the '415 patent do not teach or suggest the claimed invention. The '776 patent does not teach or suggest specific binding proteins that bind to SEQ ID NO:4 and 5. The '415 patent does not teach or suggest specific binding proteins that bind to SEQ ID NO:4. Additionally, the '415 patent does not teach or suggest that the particular sequences shown in SEQ ID NOs:4 or 5 would be useful to generate specific binding proteins that specifically bind to native canine B cell-bound IgE and which do not bind to IgE when the IgE is bound to a receptor on a mast cell. As such, the '776 patent and the '415 patent, when considered alone or combination, do not teach or suggest the claimed invention. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 17, 23, 30, and 37 Under 35 U.S.C. §103(a)

Claims 17, 23, 30, and 37 stand rejected under 35 U.S.C. §103(a) as allegedly obvious. Claims 17, 23, 30, and 37 have been canceled. Therefore, the rejection is moot. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 11, 16-17, 22-23, 29-30, 36-37, and 42-43 Under 35 U.S.C. §112, second paragraph

Claims 11, 16-17, 22-23, 29-30, 36-37, and 42-43 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite. Claims 11, 16-17, 22-23, 29-30, 36, 37 and 42 have been canceled. As such the rejection is moot as applied to these claims. Applicants respectfully traverse the rejection as it applies to claims 43.

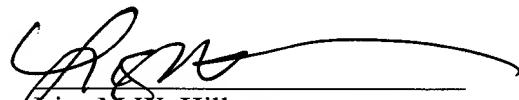
Claim 43 has been amended to remove the term “defined epitope” in favor of “epitope.” An epitope has a meaning in the art well known to those of skill in the art. The claims is therefore definite. Applicants respectfully request withdrawal of the rejection.

Conclusion

In view of the above remarks, the application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of this application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

Date: Oct 7, 2002



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APPENDIX A
Marked-Up Version of Amended Specification and Claims to Show Changes Made

IN THE SPECIFICATION:

On page 24, please replace the second full paragraph with the following paragraph:

Monoclonal antibody 8H.8 also binds to canine IgE. The 8H.8 monoclonal antibody was derived by immunizing mice with a shortened version of exon 3 of the canine IgE molecule, designated exon 3a. Exon 3a contains the C-terminal 71 amino acids of the full length exon 3. See SEQ ID NOS:33-39, and in particular SEQ ID NO:38 and 39. Previous studies (data not presented herein) had shown that immunizing mice with the full length exon 3 did not generate antibodies having specificity such as that ultimately found with the 8H.8 antibody.

IN THE CLAIMS:

6. (Three Times Amended) A specific binding protein selected from the group consisting of a monoclonal antibody, a polyclonal antibody, an antigen-binding fragment of a monoclonal antibody, an antigen-binding fragment of a polyclonal antibody, a hybrid antibody, and a single chain antibody, which specifically binds to an isolated and purified peptide [comprising] consisting essentially of SEQ ID NO:4.

15. (Twice Amended) A specific binding protein selected from the group consisting of a monoclonal antibody, a polyclonal antibody, an antigen-binding fragment of a monoclonal antibody, an antigen-binding fragment of a polyclonal antibody, a hybrid antibody, and a single chain antibody which specifically binds an isolated and purified peptide comprising an amino acid sequence which [comprises] consists essentially of Thr-Leu-Leu-Glu-Tyr-Arg-Met (SEQ ID NO:4), or a variant thereof, wherein the variant comprises an amino acid substitution at amino acid positions [4, 5, or both 4 and 5] 3, 4, or both 3 and 4.

21. (Three Times Amended) A specific binding protein selected from the group consisting of a monoclonal antibody, a polyclonal antibody, an antigen-binding fragment of a monoclonal antibody, an antigen-binding fragment of a polyclonal antibody, a hybrid antibody, and a single chain antibody, which specifically binds an isolated and purified peptide comprising an amino acid sequence which [comprises] consists essentially of Gly-Met-Asn-Leu-Thr-Trp-Tyr-Arg-Glu-Ser-Lys (SEQ ID NO:5), or a variant thereof, wherein the variant comprises an amino acid substitution at amino acid position number 5, 6, or both 5 and 6.

27. (Three Times Amended) A specific binding protein selected from the group consisting of a monoclonal antibody, a polyclonal antibody, an antigen-binding fragment of a monoclonal antibody, an antigen-binding fragment of a polyclonal antibody, a hybrid antibody, and a single chain antibody, which is raised to a multiply antigenic peptide comprising multiple copies of an isolated and purified peptide which [comprises] consists essentially of SEQ ID NO:4, SEQ ID NO:5, or both SEQ ID NO:4 and SEQ ID NO:5.

34. (Three Times Amended) A specific binding protein selected from the group consisting of a monoclonal antibody, a polyclonal antibody, an antigen-binding fragment of a monoclonal antibody, an antigen-binding fragment of a polyclonal antibody, a hybrid antibody, and a single chain antibody, which is raised to a recombinant plant virus particle comprising at least one copy of an isolated and purified peptide [comprising] consisting essentially of SEQ ID NO:4, SEQ ID NO:5, or both SEQ ID NO:4 and SEQ ID NO:5.

41. (Amended) A monoclonal antibody produced by [which is] hybridoma 8H.8 having ATCC accession number PTA-4597.

43. (Three Times Amended) A specific binding protein selected from the group consisting of a monoclonal antibody, a polyclonal antibody, an antigen-binding fragment of a monoclonal antibody, an antigen-binding fragment of a polyclonal antibody, a hybrid antibody, and a single chain antibody, which specifically binds to [the defined] an epitope bound by the antibody of claim 41.

116. (New) A specific binding protein selected from the group consisting of a monoclonal antibody, a polyclonal antibody, an antigen-binding fragment of a monoclonal antibody, an antigen-binding fragment of a polyclonal antibody, a hybrid antibody, and a single chain antibody, which specifically binds to an isolated and purified peptide consisting essentially of SEQ ID NO:39.

117. (New) A specific binding protein selected from the group consisting of a monoclonal antibody, a polyclonal antibody, an antigen-binding fragment of a monoclonal antibody, an antigen-binding fragment of a polyclonal antibody, a hybrid antibody, and a single chain antibody which specifically binds an isolated and purified peptide comprising an amino acid sequence which consists essentially of SEQ ID NO:39, or a variant thereof, wherein the variant comprises an amino acid substitution at amino acid positions 5, 6, or both 5 and 6.